EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	67	isovaleramide	USPAT	OR	ON	2007/03/16 14:13
L2	0	isovaleramice	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/03/16 14:14
L3	152	isovaleramide	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/03/16 14:14
L4	56640	seizure or epilep$ or convuls$	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2007/03/16 14:15
L5	44	l3 and l4	US-PGPUB; USPAT; EPO; JPO; DERWENT	AND	ON	2007/03/16 14:19
L6	24592	headache	US-PGPUB; USPAT; EPO; JPO; DERWENT	AND	ON	2007/03/16 14:19
L7	5	l1 and l6	US-PGPUB; USPAT; EPO; JPO; DERWENT	AND	ON	2007/03/16 14:19
S1	64	isovaleramide	USPAT	AND	ON	2006/08/29 09:29
S2	11890	convulsive adj disorder or seizure	USPAT	OR	ON	2007/03/16 14:13
S3	3	S1 and S2	USPAT	AND	ON	2006/08/29 09:27
S4	0	S1 near S2	USPAT	AND	ON	2006/08/29 09:28
S5	0	S1 near S2	USPAT	NEAR	ON	2006/08/29 09:28
S6	12900	headache or migraine	USPAT	OR	ON	2006/08/29 09:28
S7	5	S1 and S6	USPAT	AND	ON	2006/08/29 09:28

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=> s isovaleramide
           216 ISOVALERAMIDE
             2 ISOVALERAMIDES
L1         216 ISOVALERAMIDE
               (ISOVALERAMIDE OR ISOVALERAMIDES)

=> s seizure or epilep?
         15266 SEIZURE
         16594 SEIZURES
         23443 SEIZURE
                 (SEIZURE OR SEIZURES)
         22369 EPILEP?
L2       36670 SEIZURE OR EPILEP?

=> s l1 and l2
L3           8 L1 AND L2

=> d ti au abs so py 1-8

L3   ANSWER 1 OF 8  CAPLUS  COPYRIGHT 2007 ACS on STN
TI   Novel isovaleramide forms, compositions thereof, and related
     methods of use
IN   Oliveira, Mark; Peterson, Matthew
AB   The invention provides novel isovaleramide forms comprising
     isovaleramide co-crystals, and solvates, hydrates, and polymorphs
     thereof.  The invention also provides novel compns. comprising these novel
     forms and one or more suitable carriers, as well as related methods for
     the treatment or prevention of a number of conditions, including, for
     example, epilepsy and anxiety.  Thus, isovaleramide
     (49.3 mg, 0.487 mmol), gentisic acid (58.9 mg, 0.382 mmol), and methanol
     (0.120 mL) were combined and heated to 60° to form a solution  Once
     all solids were dissolved the was left to cool to room temperature forming
space
     filling needle-shaped crystals.  The resulting product was collected in a
     centrifuge filter, dried under a vacuum and characterized by DSC, TGA, IR,
     PXRD, and Raman spectra.
SO   PCT Int. Appl., 61pp.
     CODEN: PIXXD2
PY   2006
     2007
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L3 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
TI Natural ligand of G protein coupled receptor RCC356 and uses thereof
IN Sallman, Frederic; Veithen, Alex; Philippeau, Magali
AB The invention relates to the identification of isovaleric acid as a natural ligand of the RCC356 G-protein coupled receptor (GPCR). The invention encompasses the use of the interaction of RCC356 polypeptides and isovaleric acid as the basis of screening assays for agents that modulate the activity of the RCC356 receptor. The invention also encompasses diagnostic and other assays performed based upon the RCC356/isovaleric acid interaction, as well as kits for performing diagnostic and screening assays.
SO PCT Int. Appl., 79pp.
CODEN: PIXXD2
PY 2006
2006

L3 ANSWER 3 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
TI Diverse mechanisms of antiepileptic drugs in the development pipeline
AU Rogawski, Michael A.
AB A review. There is a remarkable array of new chemical entities in the current antiepileptic drug (AED) development pipeline. In some cases, the compds. were synthesized in an attempt improve upon the activity of marketed AEDs. In other cases, the discovery of antiepileptic potential was largely serendipitous. Entry into the pipeline begins with the demonstration of activity in one or more animal screening models. Results from testing in a panel of such models provide a basis to differentiate agents and may offer clues as to the mechanism. Target activity may then be defined through cell-based studies, often years after the initial identification of activity. Some pipeline compds. are believed to act through conventional targets, whereas others are structurally novel and may act by novel mechanisms. Follow-on agents include the levetiracetam analogs brivaracetam and seletracetam that act as SV2A-ligands; the valproate-like agents valrocemide, valnoctamide, propylisopropyl acetamide, and isovaleramide; the felbamate analog flurofelbamate, a dicarbamate, and the unrelated carbamate RWJ-333369; the oxcarbazepine analog licarbazepine, which probably acts as a use-dependent sodium channel blockers, and its prodrug acetate BIA 2-093; various selective partial benzodiazepine receptor agonists, including ELB139, which is a pos. allosteric modulator of α3-containing GABAA receptors. A variety of AEDs that may act through novel targets are also in clin. development: lacosamide, a functionalized amino acid; talampanel, a 2,3-benzodiazepine selective noncompetitive AMPA receptor antagonist; NS1209, a competitive AMPA receptor antagonist; ganaxolone, a neuroactive steroid that acts as a pos. modulator of GABAA receptors; retigabine, a KCNQ potassium channel opener with activity as a GABAA receptor pos. modulator; the benzanilide KCNQ potassium channel opener ICA-27243 that is more selective than retigabine; and rufinamide, a triazole of unknown mechanism.
SO Epilepsy Research (2006), 69(3), 273-294
CODEN: EPIRE8; ISSN: 0920-1211
PY 2006

L3 ANSWER 4 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
TI New antiepileptic drugs that are second generation to existing antiepileptic drugs
AU Bialer, Meir
AB A review. In the last decade, 10 new antiepileptic drugs (AEDs) have been introduced that offer appreciable advantages in terms of their favorable pharmacokinetics, improved tolerability, and lower potential for drug interactions. However, despite the large therapeutic range of old and new AEDs, .apprx.30% of the patients with epilepsy are still not seizure free and, consequently, there is a substantial need to develop new AEDs. The new AEDs currently in development can be divided

into 2 categories: drugs with completely new chemical structures such as lacosamide (formally Harkoseride), Retigabine, rufinamide, and Talampanel; and drugs that are derivs. or analogs of existing AEDs that can be regarded as second-generation or follow-up compds. of established AEDs. This article focuses on the second category and thus critically reviews the following second-generation compds.: eslicarbazepine acetate or BIA-2-093 and 10-hydroxy carbazepine (carbamazepine derivs.); Valrocemide and NPS 1776 (isovaleramide; valproic acid derivs.); Pregabalin and XP13512 (Gabapentin derivs.); brivaracetam (ucb 34714) and seletracetam (ucb 44212; levetiracetam derivs.); and fluorofelbamate (a Felbamate derivative). In addition, a series of valproic acid derivs. that are currently in preclin. stage has also been evaluated because some lead compds. of this series have a promising potential to become new antiepileptics and CNS drugs. For any of these follow-up compds. to become a successful second generation to an existing AED, it has to be more potent, safer, and possess favorable pharmacokinetics, including low potential for pharmacokinetic and pharmacodynamic drug interactions.

SO Expert Opinion on Investigational Drugs (2006), 15(6), 637-647
CODEN: EOIDER; ISSN: 1354-3784
PY 2006

L3 ANSWER 5 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
TI Could valerian have been the first anticonvulsant?
AU Eadie, Mervyn J.
AB A review. Purpose: To assess the available evidence for the belief that valerian, highly recommended in the past for treating epilepsy, possessed real anticonvulsant effectiveness. Methods: Review of available literature. Results: In 1592, Fabio Colonna, in his botanical classic Phytobasanos, reported that taking powdered valerian root cured his own epilepsy. Subsequent reports of valerian's anticonvulsant effectiveness appeared. By the late 18th and early 19th centuries, it was often regarded as the best available treatment for the disorder. Valerian prepns. yield isovaleric acid, a substance analogous to valproic acid and likely to possess anticonvulsant properties, as isovaleramide does. In favorable circumstances, high valerian doses can be calculated to have sometimes provided potentially effective amts. of anticonvulsant substance for epilepsy patients. Conclusions: Valerian probably did possess the potential for an anticonvulsant effect, but the uncertain chemical composition and content of valerian prepns., and their odor and taste, made it unlikely that they could ever prove satisfactory in widespread use.

SO Epilepsia (2004), 45(11), 1338-1343
CODEN: EPILAK; ISSN: 0013-9580
PY 2004

L3 ANSWER 6 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN
TI New CNS-active drugs which are second-generation valproic acid: can they lead to the development of a magic bullet?
AU Isoherranen, Nina; Yagen, Boris; Bialer, Meir
AB A review. Valproic acid (VPA) is one of the four first line antiepileptic drugs (AEDs). VPA is also an effective drug in migraine prophylaxis and in treatment of bipolar disorders. The use of VPA is limited by its two rare but potentially life-threatening side effects, teratogenicity and hepatotoxicity, and it is the least potent of the established AEDs. Consequently, there is an incentive to develop a second-generation VPA. A successful, second-generation VPA would need to possess the following characteristics: broad-spectrum antiepileptic activity; better potency than VPA; and lack of teratogenicity and hepatotoxicity. These characteristics would give such a drug the potential to be utilized in epilepsy and other CNS disorders. Intensive research has been carried out in order to develop a second-generation VPA that would be more potent and safer than VPA. Amide derivs. of VPA have shown particular value as potential follow-up compds. and have better in-vivo performance than VPA. Several CNS-active valproylamides are more potent as

antiepileptics than VPA, they possess broad-spectrum antiepileptic activity, and have been found to be non-teratogenic in animal models. The amide analogs of VPA that emerged from structure-pharmacokinetic-pharmacodynamic relationship studies as promising second-generation compds. are: N-methyl-tetramethylcyclopropane carboxamide, (2S,3S)-valnoctamide, (R)-propylisopropyl acetamide and valproyl glycinamide. At present there are three compds. in clin. trials in patients with epilepsy that can be regarded as second-generation VPA: valproyl glycinamide, 3-methylbutanamide or isovaleramide, and SPD421 (DP-VPA). For any one of these second-generation valproic acids to become a successful follow-up compound to VPA, it has to fulfil the above criteria and also possess favorable pharmacokinetics.

SO Current Opinion in Neurology (2003), 16(2), 203-211
CODEN: CONEEX; ISSN: 1350-7540

PY 2003

L3 ANSWER 7 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

TI Treating a variety of pathological conditions, including spasticity and convulsions, by effecting a modulation of CNS activity with isovaleramide, isovaleric acid, or a related compound

IN Artman, Linda D.; Balandrin, Manuel; Smith, Robert L.

AB Prepns. and exts. of valerian, as well as isovaleramide, isovaleric acid, and certain structurally related compds. exhibit clin. significant pharmacol. properties which implicate a treatment for a variety of pathol. conditions, including spasticity and convulsions, which are ameliorated by effecting a modulation of CNS activity. The compns. in question generally are non-cytotoxic and do not elicit weakness or sedative activity at doses that are effective for the symptomatic treatment of such pathol. conditions. Convulsions in epileptics are treated by isovaleramide.

SO U.S., 23 pp., Cont.-in-part of Appl. PCT/97US/15272.
CODEN: USXXAM

PY 2003
1998
2005
2000
2000
2001
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2002
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2004

L3 ANSWER 8 OF 8 CAPLUS COPYRIGHT 2007 ACS on STN

TI Sustained-release formulations for treating CNS-mediated disorders

IN Wells, David S.; Marriott, Thomas B.; Rajewski, Lian G.; Pipkin, James D.; Haslam, John L.

AB Sustained-release compns. for delivering therapeutic concns. of isovaleramide, isovaleric acid, and certain structurally related compds. are provided for the treatment for a variety of pathol. conditions, including epilepsy and spasticity, which are ameliorated by effecting a modulation of CNS (central nervous system) activity. The ability of the compns. to sustain relatively constant levels of the drug at a therapeutic dose in the serum for extended periods of time enables a once or twice daily administration schedule. A film-coated tablet containing isovaleramide (NPS 1776) 400, xanthan gum 56, lactose monohydrate 340, magnesium stearate 4, Aquacoate ECD 24.4, hydroxypropyl Me cellulose 9.8, di-Bu sebacate 5.8 mg was prepared

SO PCT Int. Appl., 58 pp.
CODEN: PIXXD2

PY 2001
2002
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=> s headache or migraine
10156 HEADACHE
1532 HEADACHES
10932 HEADACHE
(HEADACHE OR HEADACHES)
6221 MIGRAINE
234 MIGRAINES
6269 MIGRAINE
(MIGRAINE OR MIGRAINES)
L4 12198 HEADACHE OR MIGRAINE

=> s l1 and l4
L5 5 L1 AND L4

=> d ti au abs so py 1-5

L5 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Novel isovaleramide forms, compositions thereof, and related methods of use
IN Oliveira, Mark; Peterson, Matthew
AB The invention provides novel isovaleramide forms comprising isovaleramide co-crystals, and solvates, hydrates, and polymorphs thereof. The invention also provides novel compns. comprising these novel forms and one or more suitable carriers, as well as related methods for the treatment or prevention of a number of conditions, including, for example, epilepsy and anxiety. Thus, isovaleramide (49.3 mg, 0.487 mmol), gentisic acid (58.9 mg, 0.382 mmol), and methanol (0.120 mL) were combined and heated to 60° to form a solution Once all solids were dissolved the was left to cool to room temperature forming space filling needle-shaped crystals. The resulting product was collected in a centrifuge filter, dried under a vacuum and characterized by DSC, TGA, IR, PXRD, and Raman spectra.
SO PCT Int. Appl., 61pp.
CODEN: PIXXD2
PY 2006
2007

L5 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Migraine treatments including isovaleramide compounds and serotonin agonists
IN Artman, Linda D.
AB A method is disclosed of treating a migraine headache comprising administration of at least one serotonin agonist and isovaleramide, α-Me isovaleramide, or mixts.
thereof to a patient suffering from a migraine. Method involves at least one serotonin agonist that is selected from the group consisting of sumatriptan, eleptriptan, naratriptan, rizatriptan, zolmitriptan, almotriptan, frovatriptan, ergotamine, an ergotamine derivative, and mixts. thereof.
SO U.S. Pat. Appl. Publ., 12 pp.
CODEN: USXXCO
PY 2005
2005
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2006
2006
2006

L5 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI New CNS-active drugs which are second-generation valproic acid: can they lead to the development of a magic bullet?
AU Isoherranen, Nina; Yagen, Boris; Bialer, Meir
AB A review. Valproic acid (VPA) is one of the four first line antiepileptic drugs (AEDs). VPA is also an effective drug in migraine prophylaxis and in treatment of bipolar disorders. The use of VPA is limited by its two rare but potentially life-threatening side effects, teratogenicity and hepatotoxicity, and it is the least potent of the established AEDs. Consequently, there is an incentive to develop a second-generation VPA. A successful, second-generation VPA would need to possess the following characteristics: broad-spectrum antiepileptic activity; better potency than VPA; and lack of teratogenicity and hepatotoxicity. These characteristics would give such a drug the potential to be utilized in epilepsy and other CNS disorders. Intensive research has been carried out in order to develop a second-generation VPA that would be more potent and safer than VPA. Amide derivs. of VPA have shown particular value as potential follow-up compds. and have better in-vivo performance than VPA. Several CNS-active valproylamides are more potent as antiepileptics than VPA, they possess broad-spectrum antiepileptic activity, and have been found to be non-teratogenic in animal models. The amide analogs of VPA that emerged from structure-pharmacokinetic-pharmacodynamic relationship studies as promising second-generation compds. are: N-methyl-tetramethylcyclopropane carboxamide, (2S,3S)-valnoctamide, (R)-propylisopropyl acetamide and valproyl glycinamide. At present there are three compds. in clin. trials in patients with epilepsy that can be regarded as second-generation VPA: valproyl glycinamide, 3-methylbutanamide or isovaleramide, and SPD421 (DP-VPA). For any one of these second-generation valproic acids to become a successful follow-up compound to VPA, it has to fulfil the above criteria and also possess favorable pharmacokinetics.
SO Current Opinion in Neurology (2003), 16(2), 203-211
CODEN: CONEEX; ISSN: 1350-7540
PY 2003

L5 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Treating a variety of pathological conditions, including spasticity and convulsions, by effecting modulation of CNS activity with isovaleramide, isovaleric acid, or a related compound
IN Artman, Linda D.; Balandrin, Manuel; Smith, Robert L.
AB Prepns. and exts. of valerian, as well as isovaleramide, isovaleric acid, and certain structurally related compds. exhibit clin. significant pharmacol. properties which implicate a treatment for a variety of pathol. conditions, including spasticity and convulsions, which are ameliorated by effecting a modulation of CNS activity. The compns. in question generally are non-cytotoxic and do not elicit weakness or sedative activity at doses that are effective for the symptomatic treatment of such pathol. conditions.
SO PCT Int. Appl., 60 pp.
CODEN: PIXXD2
PY 2000
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L5 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
TI Treatment of spasticity, convulsions by isovaleric acid derivative CNS depressants
IN Artman, Linda D.; Balandrin, Manuel F.
AB Prepns. and exts. of valerian, as well as isovaleramide, isovaleric acid, and its pharmaceutically acceptable salts, esters, and

substituted amides, exhibit clin. significant pharmacol. properties which implicate a treatment for a variety of pathol. conditions, including spasticity and convulsions, which are ameliorated by effecting a mild depression of CNS activity. The compns. in question generally are non-cytotoxic and do not elicit weakness or sedative activity at doses that are effective for the symptomatic treatment of such pathol. conditions.

SO PCT Int. Appl., 50 pp.
CODEN: PIXXD2

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